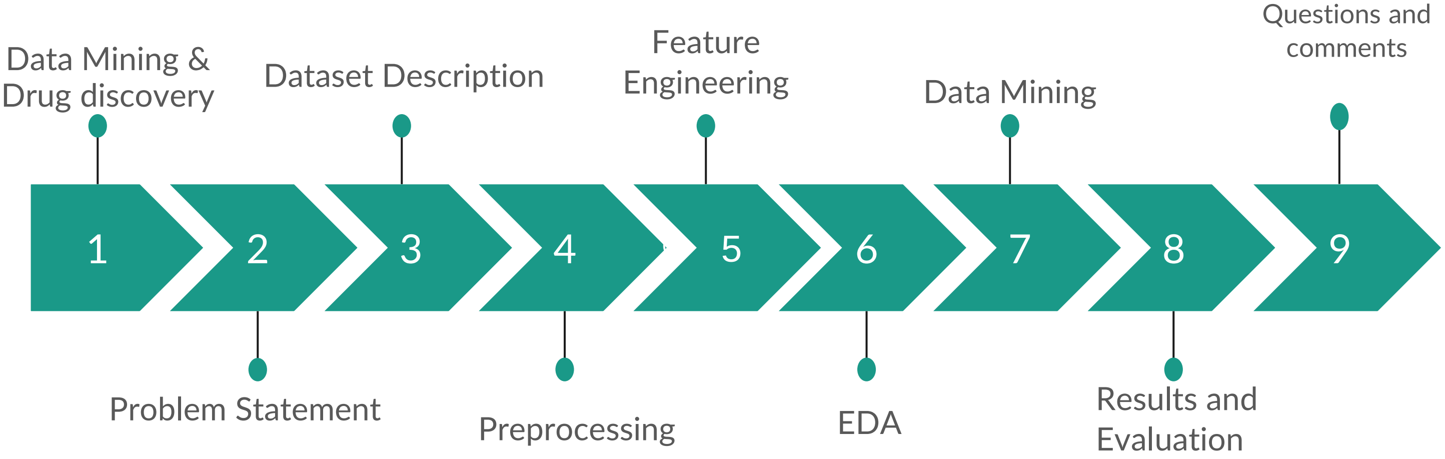
Data Mining Applications in The Healthcare field

AI-based Quantitative structure Activity relationship study (QSAR) for Alzheimer's disease

Data Mining Course –Ajman University

List of Content



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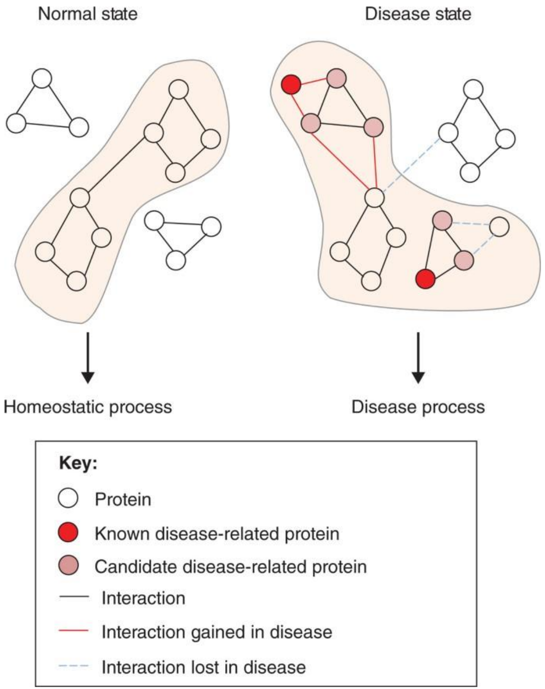
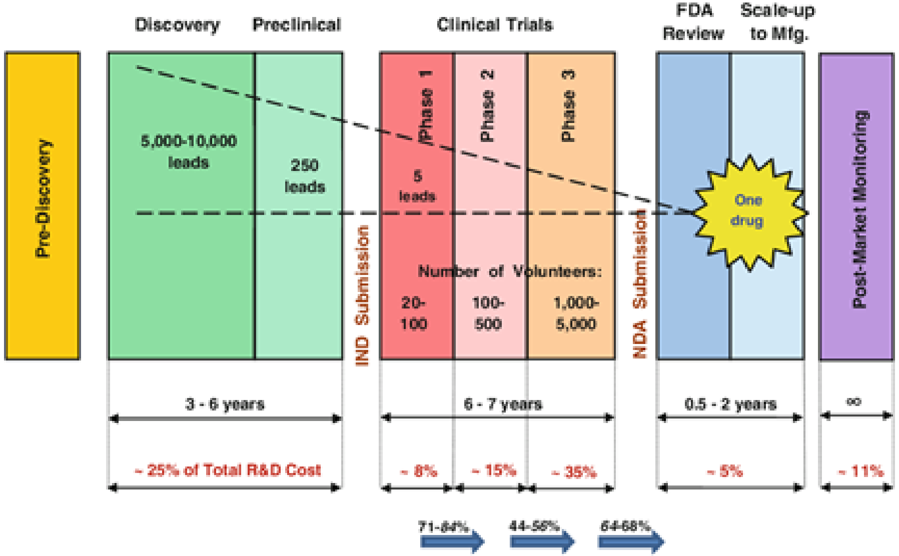
Drug Discovery & Data Mining :Story behind it

- Also called **Quantitative Structure Activity Relationship (QSAR)**
- Based on hypotheses at what is the targeted protein
- search for the molecule that changes the functionality of target protein


Normal state
Disease state
Homeostatic process
Disease process
Key:
Protein
Known disease-related protein
Candidate disease-related protein
Interaction
Interaction gained in disease
Interaction lost in disease

Drug Discovery Development Process



(Estimated Probabilities for Successful Completion of Each Phase of Clinical Trials for Pharma and Biotech Firms. The biotech firm probabilities are in *italics*.)

Problem Statement

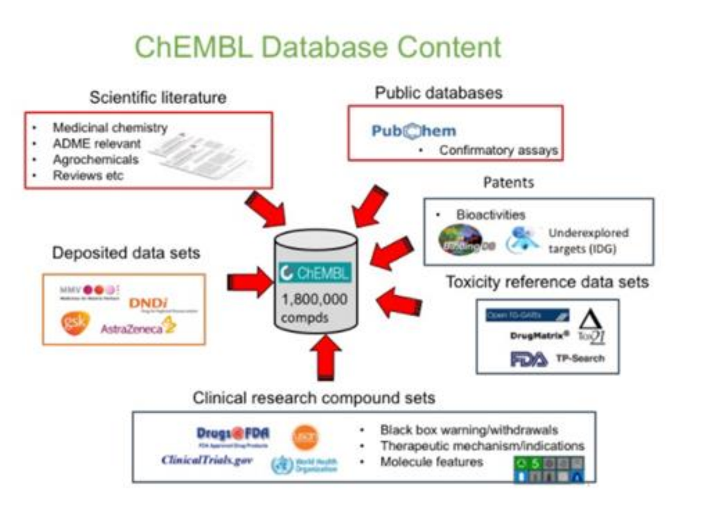
The process of drug discovery is a very long process that can take years of research, testing phases and getting the approval from Federal to be available to public for use. Utilizing Machine learning Algorithm, we aim to automate the routine work in the drug discovery laboratories of manually observing the activities of the target protein over the span of years and a load of biological calculations and analytical statistics.

Database Description

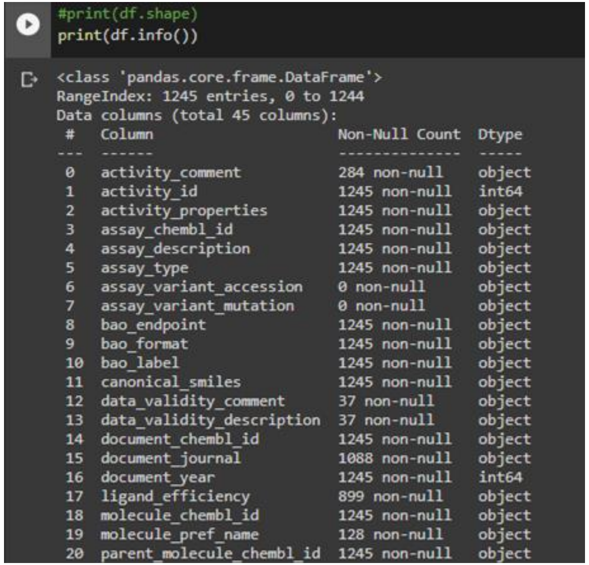
Database : ChEMBL

Disease: Alzheimer

Target protein : Amyloid Beta A4 protein

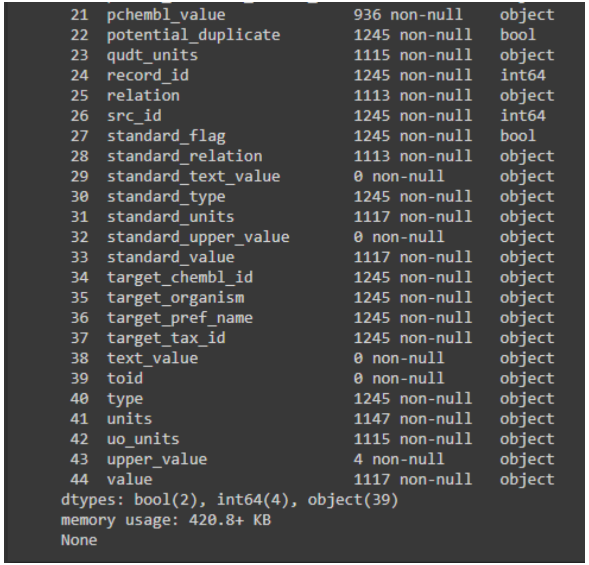


Dataset Description



```
#print(df.shape)
print(df.info())
```

```
<class 'pandas.core.frame.DataFrame'>
RangeIndex: 1245 entries, 0 to 1244
Data columns (total 45 columns):
 #   Column                     Non-Null Count  Dtype
---  ------                     --------------  -----
 0   activity_comment           284 non-null    object
 1   activity_id                1245 non-null   int64
 2   activity_properties        1245 non-null   object
 3   assay_chembl_id            1245 non-null   object
 4   assay_description          1245 non-null   object
 5   assay_type                 1245 non-null   object
 6   assay_variant_accession    0 non-null      object
 7   assay_variant_mutation     0 non-null      object
 8   bao_endpoint               1245 non-null   object
 9   bao_format                 1245 non-null   object
 10  bao_label                  1245 non-null   object
 11  canonical_smiles           1245 non-null   object
 12  data_validity_comment      37 non-null     object
 13  data_validity_description  37 non-null     object
 14  document_chembl_id         1245 non-null   object
 15  document_journal           1088 non-null   object
 16  document_year              1245 non-null   int64
 17  ligand_efficiency          899 non-null    object
 18  molecule_chembl_id         1245 non-null   object
 19  molecule_pref_name         128 non-null    object
 20  parent_molecule_chembl_id  1245 non-null   object
```

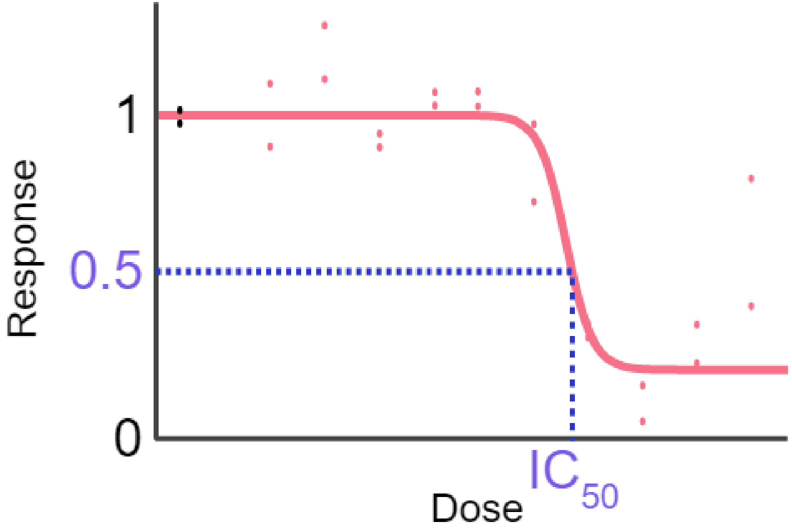


```
 21  pchembl_value              936 non-null    object
 22  potential_duplicate        1245 non-null   bool
 23  qudt_units                 1115 non-null   object
 24  record_id                  1245 non-null   int64
 25  relation                   1113 non-null   object
 26  src_id                     1245 non-null   int64
 27  standard_flag              1245 non-null   bool
 28  standard_relation          1113 non-null   object
 29  standard_text_value        0 non-null      object
 30  standard_type              1245 non-null   object
 31  standard_units             1117 non-null   object
 32  standard_upper_value       0 non-null      object
 33  standard_value             1117 non-null   object
 34  target_chembl_id           1245 non-null   object
 35  target_organism            1245 non-null   object
 36  target_pref_name           1245 non-null   object
 37  target_tax_id              1245 non-null   object
 38  text_value                 0 non-null      object
 39  toid                       0 non-null      object
 40  type                       1245 non-null   object
 41  units                      1147 non-null   object
 42  uo_units                   1115 non-null   object
 43  upper_value                4 non-null      object
 44  value                      1117 non-null   object
dtypes: bool(2), int64(4), object(39)
memory usage: 420.8+ KB
None
```

Shape = (1245, 45)

2 important attributes: canonical_smiles (obj), standard_value(obj)

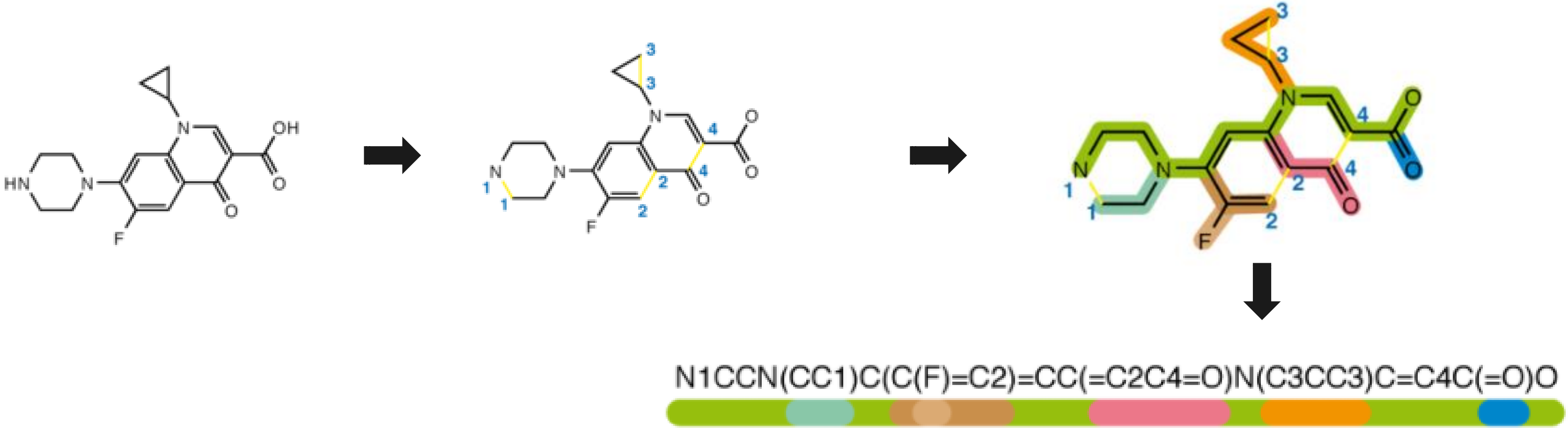
IC50 and pIC50



- Half maximum inhibition concentration :a measure of the of a potency substance in inhibiting a specific biological or biochemical function.

- pIC50 is negative log of IC50

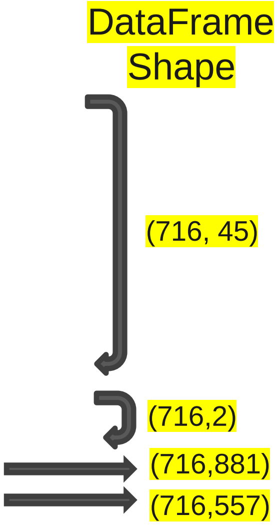
Smiles (Simplified Molecular input Line-Entry System)



N1CCN(CC1)C(C(F)=C2)=CC(=C2C4=O)N(C3CC3)C=C4C(=O)O

Data Preprocessing

1. Data Preprocessing
    a. Converted standard_value to float
    b. Drop rows that have *canonical_smiles* or\and *standard_value* as na (missing data)
    c. Drop rows that have duplicate smiles notation (duplicated data)
    d. Discritization: Create bioactivity **class** attribute and remove intermediate bioactive molecules (discritization)
    e. Simplify the smiles notation and remove non-bonded elements (remove noise)
    f. Normalize the standard value by taking the negative logarithmic value of IC50 == **pIC50** (normalization)
    g. Select The most meaningful features for our experiment [*molecule_chembl_id*, *canonical_smiles*] (feature selection)
    h. Compute **PaDEL** from the selected features (feature engineering)
    i. Eliminate non-variant features using **VarianceThreshold** method (dimension reduction)


DataFrame Shape

(716, 45)

(716,2)

(716,881)

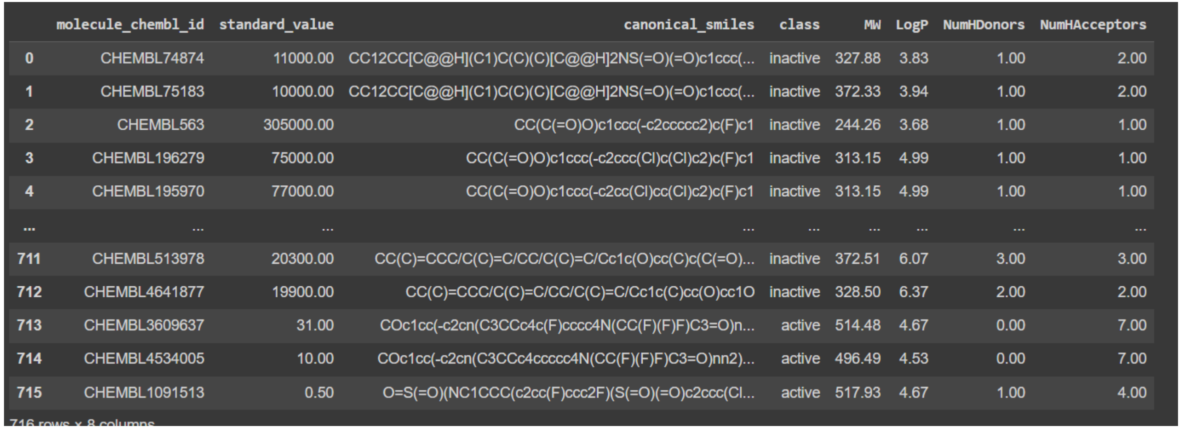
(716,557)

Feature Engineering and data splitting

2. Exploratory Data Analysis (EDA)

   Compute Lipinski descriptor and analyze the dataset in terms of **Lipinski criteria**

3. Data is split into 67% training 33% testing

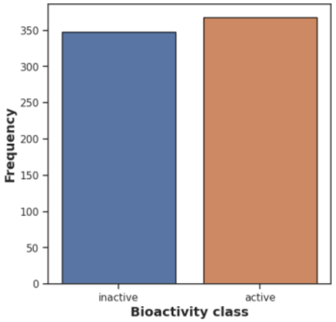


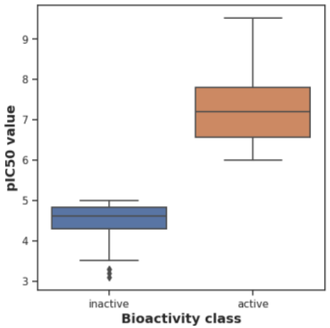
	molecule_chembl_id	standard_value	canonical_smiles	class	MW	LogP	NumHDonors	NumHAcceptors
0	CHEMBL74874	11000.00	CC12CC[C@@H](C1)C(C)(C)[C@@H]2NS(=O)(=O)c1ccc(...	inactive	327.88	3.83	1.00	2.00
1	CHEMBL75183	10000.00	CC12CC[C@@H](C1)C(C)(C)[C@@H]2NS(=O)(=O)c1ccc(...	inactive	372.33	3.94	1.00	2.00
2	CHEMBL563	305000.00	CC(C(=O)O)c1ccc(-c2ccccc2)c(F)c1	inactive	244.26	3.68	1.00	1.00
3	CHEMBL196279	75000.00	CC(C(=O)O)c1ccc(-c2ccc(Cl)c(Cl)c2)c(F)c1	inactive	313.15	4.99	1.00	1.00
4	CHEMBL195970	77000.00	CC(C(=O)O)c1ccc(-c2cc(Cl)cc(Cl)c2)c(F)c1	inactive	313.15	4.99	1.00	1.00
...	...	...	...	...	...	...	...	...
711	CHEMBL513978	20300.00	CC(C)=CCC/C(C)=C/CC/C(C)=C/Cc1c(O)cc(C)c(C(=O)...	inactive	372.51	6.07	3.00	3.00
712	CHEMBL4641877	19900.00	CC(C)=CCC/C(C)=C/CC/C(C)=C/Cc1c(C)cc(O)cc1O	inactive	328.50	6.37	2.00	2.00
713	CHEMBL3609637	31.00	COc1cc(-c2cn(C3CCc4c(F)cccc4N(CC(F)(F)F)C3=O)n...	active	514.48	4.67	0.00	7.00
714	CHEMBL4534005	10.00	COc1cc(-c2cn(C3CCc4ccccc4N(CC(F)(F)F)C3=O)nn2)...	active	496.49	4.53	0.00	7.00
715	CHEMBL1091513	0.50	O=S(=O)(NC1CCC(c2cc(F)ccc2F)(S(=O)(=O)c2ccc(Cl...	active	517.93	4.67	1.00	4.00

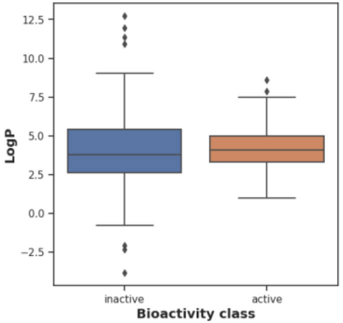
716 rows × 8 columns

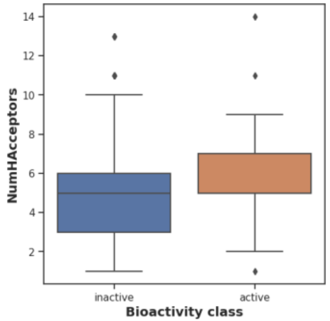
EDA

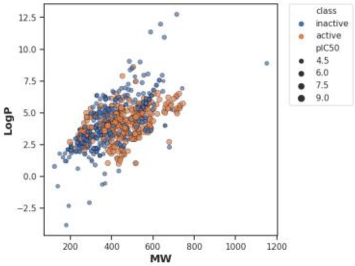
Data Exploration and Visualization using lipinski descriptors attributes

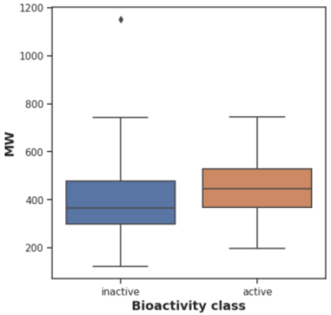


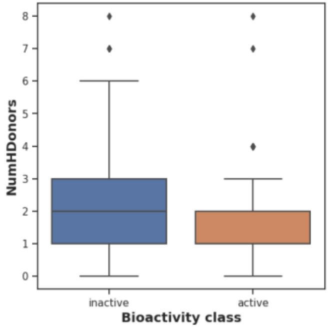




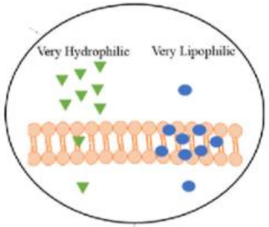




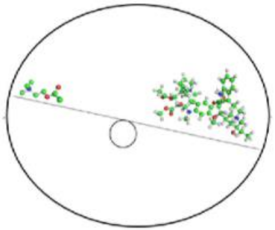




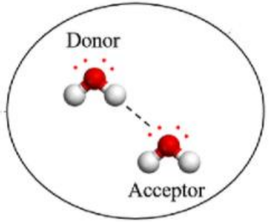
Lipinski Descriptors



Log P <5

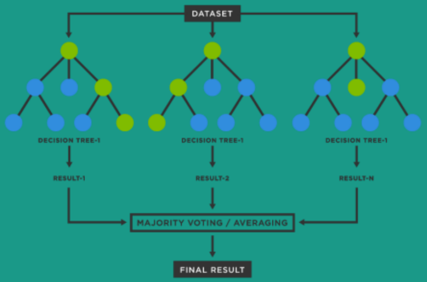


MW <500 g/mol

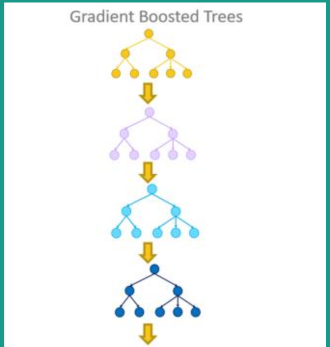


HBA <10 and HBD <5

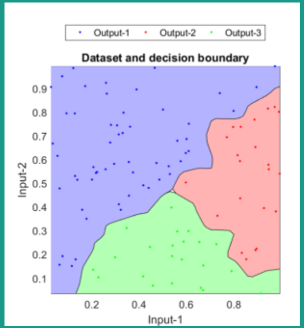
Data Mining : Regression Problem



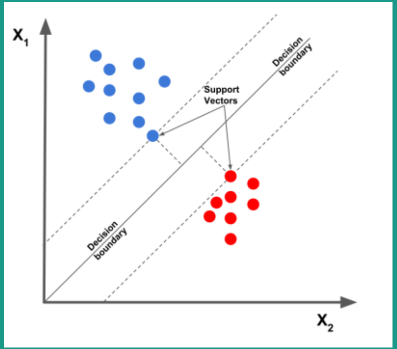
Random Forest



Gradient Boosted Regressor

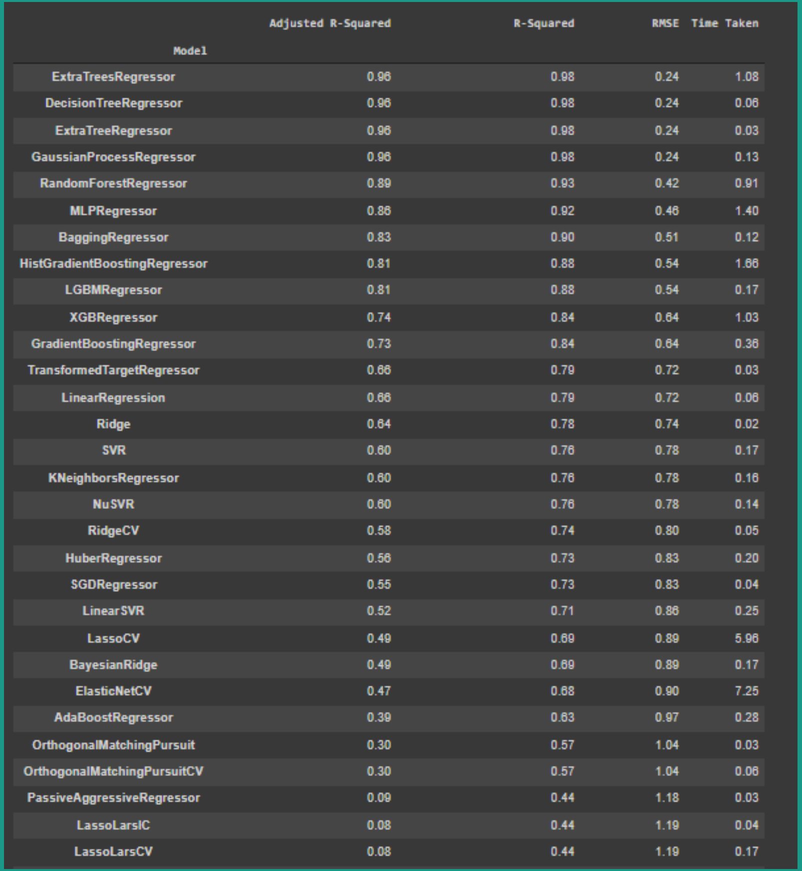


K - Nearest Neighbor

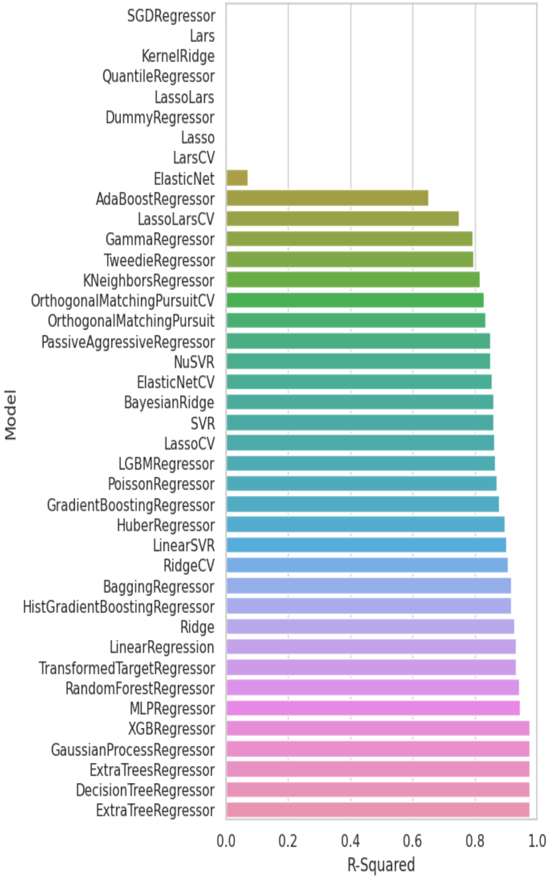


Support Vector Machine

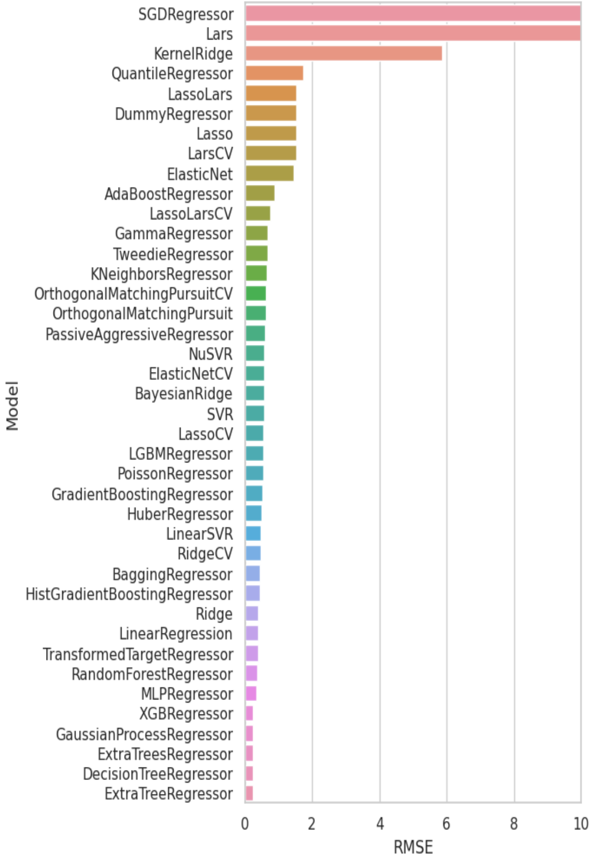
Evaluation of the Lazy Predict Models



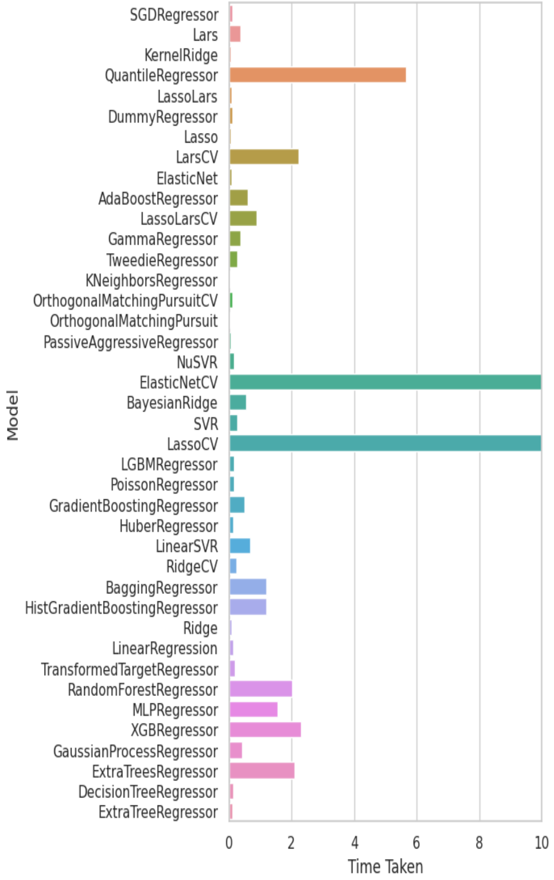
	Adjusted R-Squared	R-Squared	RMSE	Time Taken
Model				
ExtraTreesRegressor	0.96	0.98	0.24	1.08
DecisionTreeRegressor	0.96	0.98	0.24	0.06
ExtraTreeRegressor	0.96	0.98	0.24	0.03
GaussianProcessRegressor	0.96	0.98	0.24	0.13
RandomForestRegressor	0.89	0.93	0.42	0.91
MLPRegressor	0.86	0.92	0.46	1.40
BaggingRegressor	0.83	0.90	0.51	0.12
HistGradientBoostingRegressor	0.81	0.88	0.54	1.66
LGBMRegressor	0.81	0.88	0.54	0.17
XGBRegressor	0.74	0.84	0.64	1.03
GradientBoostingRegressor	0.73	0.84	0.64	0.36
TransformedTargetRegressor	0.66	0.79	0.72	0.03
LinearRegression	0.66	0.79	0.72	0.06
Ridge	0.64	0.78	0.74	0.02
SVR	0.60	0.76	0.78	0.17
KNeighborsRegressor	0.60	0.76	0.78	0.16
NuSVR	0.60	0.76	0.78	0.14
RidgeCV	0.58	0.74	0.80	0.05
HuberRegressor	0.56	0.73	0.83	0.20
SGDRegressor	0.55	0.73	0.83	0.04
LinearSVR	0.52	0.71	0.86	0.25
LassoCV	0.49	0.69	0.89	5.96
BayesianRidge	0.49	0.69	0.89	0.17
ElasticNetCV	0.47	0.68	0.90	7.25
AdaBoostRegressor	0.39	0.63	0.97	0.28
OrthogonalMatchingPursuit	0.30	0.57	1.04	0.03
OrthogonalMatchingPursuitCV	0.30	0.57	1.04	0.06
PassiveAggressiveRegressor	0.09	0.44	1.18	0.03
LassoLarsIC	0.08	0.44	1.19	0.04
LassoLarsCV	0.08	0.44	1.19	0.17



R-squared values



RMSE values

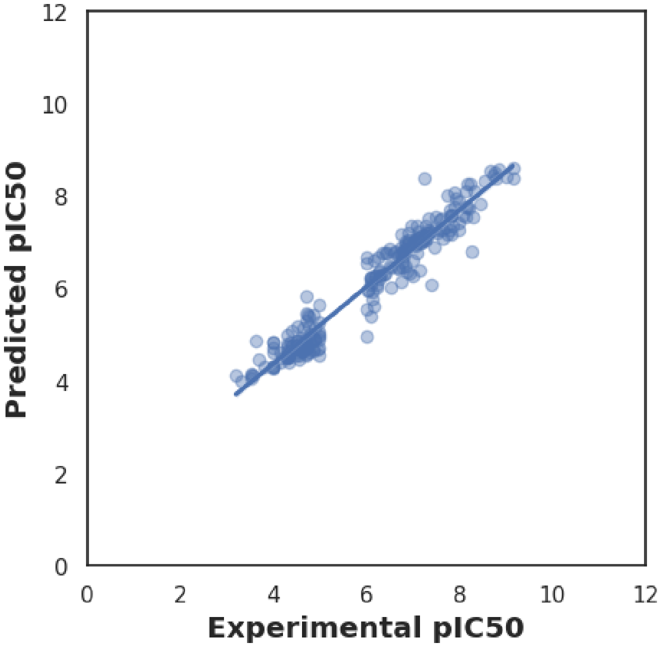


Computation Time

Hyperparameter Optimization

- Search Grid for the best performing parameters
  - Number of estimators = 800
  - Tree Depth = 8
- Cross Validation , cv = 3

Model	R2 Score	MAE	Execution time (Sec)
Random Forest	0.7045	0.549	0.0091
Gradient Boosted regressor	0.692	0.61	0.0015
K-nearest Neighbor	0.68	0.61	0.0016
Support Vector Machine	0.708	0.61	0.0018
Optimized Random Forest	0.928	0.29	0.0702



Questions & Comments

Thank you